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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,481	05/15/2008	Zissimos Mourelatos	UPN00028-100	6145

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EXAMINER	
SHIN, DANA H	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,481	MOURELATOS ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10,13-20,24,27-32,36,39-41,45 and 48-57* is/are pending in the application.

4a) Of the above claim(s) *14-20,24,27-32,36,40,41,45 and 53-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10,13,39 and 48-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2-23-2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of claims 1-6, 10 and 13 with a species election of an oncogene in the reply filed on August 6, 2009 is acknowledged. The traversal is on the ground(s) that all claims share a single inventive concept such that the claimed invention contributes a special technical feature over the prior art of Elbashir et al. as Elbashir et al. do not teach the design parameters. This is not found persuasive because the claimed siRNA identification method is encompassed by the siRNA design method of Elbashir et al. and other prior art references. See below for prior art rejections. Further, it is noted that applicant has explicitly acknowledged that the claimed inventions as grouped in the restriction/election requirement are patentably distinct from each other. See page 12 of the reply.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

Claims 1-6, 10, 13-20, 24, 27-32, 36, 40-41, 45, and 48-57 are pending in the instant application. Claims 14-20, 24, 27-32, 36, 40-41, 45, and 53-57 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Accordingly, claims 1-6, 10, 13, and 48-52 are under examination on the merits in the instant case.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on February 23, 2007 is being considered by the examiner except citation Nos. AA and AB. Note that the U.S. Patent application No. US 2003/019363 does not exist, and therefore examiner cannot locate this document. Note that US 2003/0175727 is not by Wang et al., but by Hyldig-Nielsen et al. with the title "PNA probes, probe sets, methods and kits pertaining to the detection of candida". Since examiner cannot locate the "Wang et al." reference, citation AB is not considered.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/513,489, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. It is found that the disclosure of 60/513,489 does not

provide adequate support for the claimed method steps recited in the elected claims as it is vastly devoted to the relationship between eIF2C2 and let-7, not the claimed siRNA identification methods, wherein the siRNA is targeted to an oncogene using BLAST or ENSEMBL and consists of 18, 19, 20, 21, 22, 23, 24, or 25 nucleotides in length. Accordingly, the benefit of the 60/513,489 filing date is denied and the filing date of PCT/US04/35124 (October 22, 2004) will be the effective filing date for claims 1-6, 10, 13, and 48-52.

If applicant believes that the claimed subject matter is adequately described by the disclosure of 60/513,489 in the manner provided by the first paragraph of 35 U.S.C. 112, applicant is advised to point out the particulars in response to this Office action.

Claim Objections

Claim 1 is objected to because of the following informalities: It appears that the word "nucleotides" is necessary immediately following "18-25" in line 4. Appropriate grammatical correction is required.

Claim 6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 6 depends from claim 1, which recites that the siRNA nucleotide sequence "consists of" 18-25 nucleotides. Claim 6 essentially recites the same structural limitation such that the siRNA "consists of" 18-25 nucleotides. Hence, the subject matter of claim 6 does not differ from that of claim 1, and therefore, claim 6 fails to further limit the subject matter of claim 1. Applicant is required to

cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 51 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 51 depends from claim 2, which limits the length of the siRNA nucleotide sequence to 18-24 nucleotides, wherein 24 is the maximum number of nucleotides. However, claim 51 recites that the siRNA sequence consists of 25 nucleotides, which is more than 24 nucleotides. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 and 48-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the siRNA nucleotides" in line 5. There is insufficient antecedent basis for this limitation in the claim. For examination purpose, the term "siRNA nucleotides" will be interpreted as "siRNA nucleotide sequence".

Claim 1 recites the limitation "the siRNA nucleotide" in lines 10-11 and 14. There is insufficient antecedent basis for this limitation in the claim. For examination purpose, the term "siRNA nucleotide" will be interpreted as "siRNA nucleotide sequence".

Claim 2 recites the limitation "the siRNA nucleotide" in lines 11-12 and 15-16. There is insufficient antecedent basis for this limitation in the claim. For examination purpose, the term "siRNA nucleotide" will be interpreted as "siRNA nucleotide sequence".

Claims 3-5 and 48-50 recite the limitation "the database of mRNA sequences". There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 10, 13, and 48-52 are rejected under 35 U.S.C. 102(e) as being anticipated by Liu et al. (US 2004/0091926 A1).

Liu et al. teach that one can identify an siRNA sequence that uniquely targets CLPP1 that is implicated in cancer cell growth and proliferation by identifying a 19-mer nucleotide sequence that is sequence-specific only for the CLPP1 mRNA sequence, wherein one must verify the

sequence specificity of the selected candidate siRNA against CLPP1 by accessing computer web-based databases (e.g., NCBI and ENSEMBL) and performing nucleotide homology analysis, which allows one to verify that the selected 19-mer sequence is unique to the CLPP1 mRNA sequence. They show antisense siRNA sequences of CLPP1-specific siRNAs, wherein all of 19 consecutive sequences are 100% complementary to the target sequence of CLPP1. See paragraphs 0060, 0078, 0085, 0101, 0107, 0111-0112, 0250; Tables 3-4; claims 21-22. Hence, the CLPP1-specific siRNA sequence identification method of Liu et al. inherently and necessarily comprises the method step of determining whether the 11 consecutive nucleotides from the 5'-end of the antisense strand sequence are complementary to a gene other than CLPP1, absent evidence to the contrary. Accordingly, all claim limitations are taught by Liu et al.

Claims 1-6, 13, and 48-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Elbashir et al. (*Methods,* 2002, 26:199-213, citation of record).

Elbashir et al. teach that one can identify a uniquely targeting siRNA nucleotide sequence for a target mRNA sequence comprising identifying a 19-mer target mRNA sequence that satisfies the nucleotide selection rules (e.g., 5'-AA(N19)UU; about 50% G/C content) and performing "Blast-search" via www.ncbi.nlm.nih.gov/BLAST in order to verify and ensure whether the selected candidate siRNA sequence (the entire, consecutive 19 nucleotides that are 100% identical to the target mRNA sequence) is unique such that only a single gene is targeted by the selected siRNA sequence. They teach that one synthesizes siRNA duplex comprising the siRNA sense strand sequence (the mRNA target sequence) and the siRNA antisense strand sequence that is 100% complementary to the mRNA target sequence, wherein the entire 19-mer

antisense strand sequence is 100% complementary to the mRNA target sequence. See page 202. Elbashir et al. do not explicitly teach that one need to determine whether the 11 consecutive nucleotides from the 5' end of the antisense strand sequence are complementary to the mRNA sequence other than the intended target when performing the "Blast-search". However, it necessarily and logically flows that a person performing the siRNA identification and synthesis methods of Elbashir et al. would necessarily ensure that the 11 consecutive nucleotides from the 5' end of the antisense strand sequence are complementary only to the target mRNA because Elbashir et al. taught that one should check whether the entire 19 consecutive nucleotides of the selected target sequence is unique target sequence for the selected siRNA sequence. Hence, since Elbashir et al. inherently teach all of the active method steps encompassing the claimed method steps, absent evidence to the contrary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 10, 13, and 48-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elbashir et al. (*Methods,* 2002, 26:199-213, citation of record) in view of Tuschl et al. (WO 03/099298 A1), Martinez et al. (*Cell,* 2002, 110:563-574, applicant's citation), and Ureta-Vidal et al. (*Nature Reviews Genetics,* 2003, 4:251-262).

Elbashir et al. teach that one can identify a uniquely targeting siRNA nucleotide sequence for a target mRNA sequence comprising identifying a 19-mer target mRNA sequence that satisfies the nucleotide selection rules (e.g., 5'-AA(N19)UU; about 50% G/C content) and performing "Blast-search" via www.ncbi.nlm.nih.gov/BLAST in order to verify and ensure whether the selected candidate siRNA sequence is unique such that only a single gene is targeted by the selected siRNA sequence. They teach that one synthesizes siRNA duplex comprising the siRNA sense strand sequence (the mRNA target sequence) and the siRNA antisense strand sequence that is complementary to the mRNA target sequence, wherein the entire 19-mer antisense strand sequence is complementary to the mRNA target sequence. See page 202. Elbashir et al. do not explicitly teach determining whether additional mRNA sequence in the BLAST database are complementary to an 11 consecutive nucleotides of the antisense strand sequence of the siRNA including the third nucleotide from the 5' end of the antisense strand sequence, wherein the siRNA is targeted to an oncogene.

Tuschl et al. teach that one can identify siRNA target sequences that uniquely target a specific oncogene such as Ras, Src, Jnak, Raf, c-Myc, anc Bcl-2 by selecting a 19-mer sequence that is target-specific, wherein most preferably, the antisense strand sequence of the siRNA is

100% complementary to the target mRNA sequence. They teach that the oncogene-specific siRNAs can be used in cancer therapeutic methods. They show that siRNAs mediate RNAi by cleaving target mRNA at a position between nucleotide 10 and 11 of the target mRNA that is complementary to the antisense strand sequence of an siRNA, wherein the nucleotide position is counted from the 5' end of the antisense (guide) strand sequence having at least 11 consecutive nucleotides complementary to the target mRNA sequence from the 5' end. They demonstrate that altered, non-target sequence complementary antisense sequences of an siRNA significantly reduce RNAi activity of the siRNA. See the entire reference including Figures 15-16 and 18.

Martinez et al. teach that single-stranded, antisense (guide strand) siRNAs mediate RNAi just like double-stranded siRNAs by cleaving target mRNAs, wherein the RISC-dependent target mRNA cleavage occurs at a position between nucleotides 10 and 11 when counted from the 5' end of the antisense strand sequence. They teach that the target mRNA-complementary, antisense siRNAs can be 19-25 nucleotides in length. See the entire reference.

Ureta-Vidal et al. teach that genomic, mRNA, and protein sequence databases are available at the Ensembl and NCBI websites. See the entire reference.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the siRNA sequence identification method of Elbashir et al. by incorporating the teachings of the prior art references cited herein.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success so as to identify an oncogene-specific siRNA sequence and synthesize the oncogene-specific siRNA molecule for potential use in cancer therapeutics as suggested by Tuschl et al., because oncogene-specific siRNA sequences that only target a specific type of

oncogene were known to be identifiable as taught by Tuschl et al., wherein one is equipped with computer-based online access to publicly available sequence homology databases such as NCBI and Ensembl. Since 100% sequence complementarity between the target mRNA sequence and the antisense strand sequence of an siRNA molecule was an art-recognized preferred sequence homology parameter for siRNA selection and synthesis as taught by Elbashir et al., Tuschl et al., and Martinez et al., and since sequence alterations in the antisense strand sequence of siRNAs were known to significantly decrease the RNAi activity level of siRNA molecules as demonstrated by Tuschl et al., and since the RISC-mediated target mRNA cleavage was known to occur between nucleotides 10 and 11 when counted from the 5' end of the antisense strand sequence, it would have been apparent to one of ordinary skill in the art to ensure that all 11 consecutive nucleotides (e.g., nucleotide positions 1-11 from the 5' end of the antisense strand) as well as all 19 consecutive nucleotides of the antisense strand sequence are 100% complementary to the target mRNA sequence for specific RNAi-mediated oncogene silencing and for effective siRNA-based cancer therapeutics. Since all skills, information, and knowledge required to arrive at the claimed invention were known in the art at the time the application was filed, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner
Art Unit 1635

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